

## PCT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

LENTZ, Nelsen, L.  
Eli Lilly And Company  
Lilly Corporate Center  
Indianapolis, IN 46285  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 11 March 2002 (11.03.02)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference X-12968	
International application No. PCT/US00/20824	International filing date (day/month/year) 14 September 2000 (14.09.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address LIANG, Sidney, Xi 8430 Harrison Parkway Fishers, IN 46038 United States of America	State of Nationality CN	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input checked="" type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address LIANG, Sidney, Xi 79 Carriage Drive Bethany, CT 06524 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer François BAECHLER
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 13 June 2001 (13.06.01)	
<b>International application No.</b> PCT/US00/20824	<b>Applicant's or agent's file reference</b> X-12968
<b>International filing date</b> (day/month/year) 14 September 2000 (14.09.00)	<b>Priority date</b> (day/month/year) 29 September 1999 (29.09.99)
<b>Applicant</b> KOHLMAN, Daniel, Timothy et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

03 April 2001 (03.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Charlotte ENGER Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: <span style="float: right; font-size: 1.5em; font-weight: bold;">RECEIVED</span> LENTZ, Nelson L. <span style="float: right; font-size: 1.5em; font-weight: bold;">PCT</span> ELI LILLY AND COMPANY Lilly Corporate Center Indianapolis, IN 46285 ETATS-UNIS D'AMERIQUE <div style="text-align: center; margin-top: 10px;">             JUL 12 2001              ELI LILLY &amp; COMPANY              PATENT DIVISION           </div>		NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)	
Applicant's or agent's file reference X-12968		<b>IMPORTANT NOTIFICATION</b>	
International application No. PCT/US00/20824	International filing date (day/month/year) 14/09/2000	Priority date (day/month/year) 29/09/1999	
Applicant ELI LILLY AND COMPANY et al.			

**BEST AVAILABLE COPY**

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/  <div style="display: flex; align-items: center;"> <div>             European Patent Office              D-80298 Munich              Tel. +49 89 2399 - 0 Tx: 523656 epmu d              Fax: +49 89 2399 - 4465           </div> </div>	Authorized officer  Oberhauser, A  Tel. +49 89 2399-8139
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REC'D 23 OCT 2001

EPO

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference X-12968	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/20824	International filing date (day/month/year) 14/09/2000	Priority date (day/month/year) 29/09/1999
International Patent Classification (IPC) or national classification and IPC C07D409/14		
Applicant ELI LILLY AND COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  03/04/2001	Date of completion of this report  06.07.2001
Name and mailing address of the International preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Papathoma, S  Telephone No. +49 89 2399 7536  

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20824

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-103 as originally filed

**Claims, No.:**

1-20 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20824

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 12-14.

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-20
	No: Claims
Inventive step (IS)	Yes: Claims 1-20
	No: Claims
Industrial applicability (IA)	Yes: Claims 1-11, 15-20

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/20824

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No:      Claims

2. Citations and explanations  
**see separate sheet**

**VI.      Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

For the assessment of the present claims 12-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: PATENT ABSTRACTS OF JAPAN vol. 018, no. 046 (C-1157), 25 January 1994 (1994-01-25) & JP 05 271220 A (AJINOMOTO CO INC), 19 October 1993 (1993-10-19)
- D2: WO 99 05140 A (MIKKELSEN IVAN ;LUNDBECK & CO AS H (DK); MOLTZEN EJNER KNUD (DK);) 4 February 1999 (1999-02-04)
- D3: EP-A-0 812 826 (LILLY CO ELI) 17 December 1997 (1997-12-17)

The application refers to piperidine derivatives of the formula I suitable for inhibiting the reuptake of serotonin and antagonizing the serotonin receptor.



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/20824

**1) Article 33(2) PCT**

Although the prior art documents refer to similar compounds, the ones of the application were not disclosed in any of them. Therefore the compounds of the application, their pharmaceutical compositions, their uses and the methods of treatment comprising their administration are novel according to the Article 33(2) PCT.

**2) Article 33(3) PCT**

From the prior art documents D1 is considered to be the closest prior art, since its compounds, and particularly, the compounds 5, 22, 31, 32, 36, 37, 38, 39, 43, and 44, are the structurally closest more related compounds to the ones of the application and moreover they show antiserotonic activity.

However by the compounds of the application the R<sup>4</sup> substituent can be an aryl, cycloalkyl etc. group, while the ones of D1 have in the corresponding position a CN group as substituent.

The CN-substitution of the compounds of D1 can not be considered to make obvious a substitution by a cyclic moiety (aryl etc.), as proposed in the application.

Therefore the compounds of the application, their pharmaceutical compositions, their uses and the methods of treatment comprising their administration are considered to be inventive according to the Article 33(3) PCT.

**Re Item VI**

**Certain documents cited**

Document D4:

D4: EP-A-0 982 304 (LILLY CO ELI) 1 March 2000 (2000-03-01)

can not be considered as prior art document under the Article 33(2) PCT, because it is published after the priority day and before the filing day of the application. However care should be taken by the applicant while entering the regional phase, because this document could be relevant for the examination, as it refers to similar piperidine derivatives having effects on serotonin related systems.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>X-12968</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/ 20824</b>	International filing date (day/month/year) <b>14/09/2000</b>	(Earliest) Priority Date (day/month/year) <b>29/09/1999</b>
Applicant  <b>ELI LILLY AND COMPANY</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- ☐ the text is approved as submitted by the applicant.
- ☒ the text has been established by this Authority to read as follows:

**PIPERIDINE DERIVATIVES AS REUPTAKE INHIBITORS**

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.

☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

/US 00/20824

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C07D409/14 C07D409/04 C07D405/14 C07D405/04 A61K31/443  
 A61K31/4436 A61P25/24

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PATENT ABSTRACTS OF JAPAN vol. 018, no. 046 (C-1157), 25 January 1994 (1994-01-25) & JP 05 271220 A (AJINOMOTO CO INC), 19 October 1993 (1993-10-19) abstract ---	1,11,12, 14-20
A	WO 99 05140 A (MIKKELSEN IVAN ;LUNDBECK & CO AS H (DK); MOLTZEN EJNER KNUD (DK);) 4 February 1999 (1999-02-04) claims 1-19 ---	1,11-20
A	EP 0 812 826 A (LILLY CO ELI) 17 December 1997 (1997-12-17) claims 1-8 ---	1,11-20
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	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## ° Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

26 February 2001

Date of mailing of the international search report

08/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Bader, K

## INTERNATIONAL SEARCH REPORT

International Application No

/US 00/20824

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	EP 0 982 304 A (LILLY CO ELI) 1 March 2000 (2000-03-01) claims 1-32 -----	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/US 00/20824

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
JP 05271220	A	19-10-1993	NONE		
<hr/>					
WO 9905140	A	04-02-1999	AU	8534098 A	16-02-1999
			BR	9810790 A	25-07-2000
			CN	1265107 T	30-08-2000
			EP	1007523 A	14-06-2000
			NO	20000372 A	21-03-2000
			PL	338194 A	09-10-2000
			ZA	9806237 A	31-03-1999
<hr/>					
EP 0812826	A	17-12-1997	AU	3390797 A	07-01-1998
			BR	9709726 A	10-08-1999
			CA	2256649 A	18-12-1997
			EP	1077213 A	21-02-2001
			JP	2000512296 T	19-09-2000
			WO	9747302 A	18-12-1997
			US	6046215 A	04-04-2000
			US	5846982 A	08-12-1998
<hr/>					
EP 0982304	A	01-03-2000	AU	4726699 A	17-01-2000
			WO	0000198 A	06-01-2000
<hr/>					